UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,768	05/04/2005	Piero Chiarelli	0002263USU/3061	8171

27623 7590 08/05/2010

OHLANDT, GREELEY, RUGGIERO & PERLE, LLP
ONE LANDMARK SQUARE, 10TH FLOOR
STAMFORD, CT 06901

EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
08/05/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,768	CHIARELLI ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-36 and 38-50* is/are pending in the application.

4a) Of the above claim(s) *46-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-36 and 38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/3/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 3, 2010 has been entered.

2. Applicants' arguments, filed June 3, 2010, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 – 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 36 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. None of the cellulose derivatives other than those explicitly recited (e.g., alkyl-cellulose and hydroxyalkyl cellulose) meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus of derivatives of cellulose encompassed by the claim, since there is no description of the structural relationship of these derivatives provided in the specification and Applicant has not provided a description as to how the base molecule may be changed while remaining a derivative of cellulose.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 34 – 36, 38 – 42 and 44 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanios (US 2002/0004065). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed April 6, 2009, December 4, 2009 and those set forth below.

Applicants argue that they have clearly identified the field of endeavor by indicating that the claimed devices are designed to make possible the use of rifaximin "outside the intestine (e.g., in the oral and pharyngeal or nasal cavity, in the rectum and vagina)" and was reported in the specification. The current invention relates to a device for the controlled local delivery of rifaximin, where "local delivery" means "topical delivery". Local use of rifaximin allows the use of high concentrations with a great

efficacy, a null systemic concentration and therefore collateral effects which means that no transdermal delivery takes place. These arguments are unpersuasive. The field of endeavor and the arts to which one skilled in the art would look is broader than the very narrow definition given by applicant. In looking at ways to deliver rifaximin, one of ordinary skill in the art would look at known rifaximin devices/dosages but also drug delivery devices/forms known in the art that could be used to deliver rifaximin. Kanios et al. falls within that larger area. Also, the application as filed does not define "local delivery" to be limited to "topical delivery" and the customary definition of local delivery known to a person of ordinary skill in the art could include for example, drug releasing implants like stents, which provide for a local delivery of an active agent but not topical delivery.

Applicants also argue that Kanios provides for transdermal delivery that achieves a substantially zero order drug release profile independent of the drug used. Kanios also fails to disclose the most relevant technical features of the currently claimed device. In is “no more than an accidental case” that rifaximin is randomly listed among dozens of antibacterial drugs and Kanios et al. clearly describes that his device is absolutely independent of the drug. These arguments are unpersuasive. A drug release profile for the device is not recited in the instant claims. While the claims use the term “biphasic” that in some situations can refer to the phases of drug release, but when examined as a whole, the term “biphasic material” in the instant claims refers to the components of the device that includes both a solid phase and a liquid phase. As was discussed previously, the device of Kanios is taught as being useful for the delivery of

many active agents and thus one of ordinary skill would have been motivated to prepare the claimed device with each of the recited drugs if they were interested in preparing a device to deliver one of those active ingredients. That the device can be used to deliver many different drugs does not negate the teaching that the disclosed device can be used to deliver any one of the listed drugs.

Applicants also argue that Kanios gave a scientifically incorrect teaching of being able to transdermally administer rifaximin. Two cited documents are provide that teach that "rifaximin is not absorbed, i.e. does not pass the skin to be systemically delivered, since no detectable amounts have been found in blood and urine, thus limiting the external use of Rifaximin to topical administration." (p 9 of response, emphases omitted). These arguments are unpersuasive. The cited documents do in fact show that upon topical application of rifaximin, the substance was not detected in the blood or urine. Points 9 and 10 of the Summary Report for rifaximin by the Committee for Veterinary Medicinal Products (one of the documents submitted by Applicant) indicates that topical application resulted in rifaximin being present in the skin but not in the muscle and fat underlying the treatment areas. These are insufficient to indicate that no skin penetration occurs. Substances can pass through the skin and either because of insufficient quantity or because the substance is not transported far enough into the skin to reach the circulatory system so that such agents can be transdermally absorbed but not be detected in either the blood or urine. In the absence of evidence regarding the ability of rifaximin to pass through the skin by more direct experiments with greater

detail as tow hat was assayed, this line of argument is unpersuasive. It is also noted that the preamble of the claim only requires local delivery and not systemic delivery.

Applicant again argues that PVA is part of an unlimited list of possible crystallization inhibitors but in the subsequent paragraphs only PVP is actually taught as suitable and efficiently used as crystallization inhibitor. These arguments are unpersuasive. As discussed in the previous Office Action, the teachings of reference are not limited to the examples but are prior art for all that they teach. The number of explicitly identified substances useful as crystallization inhibitor is relatively short and includes PVA. The reference does not teach away from PVA even though it is not used in the example as PVA is not criticized, discredited or otherwise discouraged (see MPEP 2123).

Applicants also argue that Kanios et al. only demonstrates enablement for hormones, specifically estradiol and norethindrone acetate, and chemistry, pharmaceuticals and biotechnology are recognized unpredictable art fields. These arguments are unpersuasive. The predictability or unpredictability of the filed is only one of the 8 factors of *In re Wands* and Applicants remark about one of the eight factors in insufficient to establish a lack of enablement for the reference.

Applicants also wonder “why in the Claim 34 should readable both the essential features and the results achieved therefrom, even considering the latter as such have non-limiting character." (p 11, ¶ 1). This argument is not completely understood by the Examiner but as can best be understood, Applicant could be arguing that claim 34 should not have to recite the essential features and the results. Such an argument is

unpersuasive. The essential elements are the physical elements recited in the claim which are taught by the cited prior art. Applicants have not presented any evidence commensurate in scope with the claims as to the unexpected results achieved by the present composition in comparison with the closest prior art. If this argument is not what Applicant meant, additional clarification regarding this argument is required.

Applicants are “still persuaded that the Examiner came to her conclusion on the basis of hindsight reconstruction” (p 11, last paragraph, emphasis omitted). Applicants allege that the Examiner has not taken into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made and included knowledge gleaned only from Applicants" disclosure while relying on a scientifically incorrect teaching. These arguments remain unpersuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The entire teachings of Kanios disclosing both rifaximin and the crystallization inhibitor is prior art and has not been established to be scientifically incorrect as alleged by applicant.

9. Claims 34 – 36 and 38 – 44 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanios further in view of Govil et al. (US 4,908,213). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed April 6, 2009, December 4, 2009 and those set forth herein.

Additional arguments regarding this rejection by Applicant are that Govil et al. related to transdermal drug delivery systems and so does not pertain to the same field of endeavor as the current invention. This argument is unpersuasive. The secondary reference need not be completely analogous to the claimed invention but rather combinable with the primary reference and analogous art can be combined to render the claims obvious. The Govil et al. reference is clearly analogous to the Kanios reference as both relate to transdermal drug delivery system. As such, these two references are properly combinable and the combination of these two references yields the device of the instant claims.

Applicant also argues that the skilled artisan would not have found any useful information for the problem associated with topical rifaximin use for a patch comprising nicotine and at least one antipruritic compound to reduce or eliminate the itching caused by the transdermal penetration of nicotine. The inclusion of any acrylic polymer does not add anything useful for the skilled person, unless acknowledging further hindsight reconstruction of the present invention. These arguments are unpersuasive. The person of ordinary skill in the art would look to Govil et al. as providing additional information regarding the polymeric materials that can be used as pharmaceutically acceptable

pressure sensitive adhesives in transdermal drug devices such as those disclosed by Kanios.

10. Claims 34 – 36, 38 – 42, 44 and 45 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kanios further in view of Wharton (US 6,194,455). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed April 6, 2009, December 4, 2009 and those set forth herein.

Additional arguments regarding this rejection by Applicant are that Wharton clearly and expressly does not pertain to the same field of endeavor as the current invention as it relates to preventing a nascent herpes outbreak from developing into an ulcer. Wharton et al. discloses a combination of sucralfate and lidocaine and a pharmaceutically effective amount of an antibiotic but does not generally disclose a combination of an antibiotic with another antibiotic and/or an anti-inflammatory and/or pain reliever and/or anesthetic drug. These arguments are unpersuasive. The composition by which Wharton achieves the treatment effects are through the application to the skin of pharmaceutically active ingredient containing compositions. As both Kanios and Wharton are drawn to application to the skin of active ingredient containing composition, the pieces of art can be combined. Only one embodiment within the scope of the claims is required to render the claim obvious. Because of the "and/or" connectors, the combination of anti-ulcer medicine (sucralfate) with an antibiotic and the anesthetic lidocaine is sufficient to render the claim obvious.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nissa M Westerberg/
Examiner, Art Unit 1618